REMARKS

I. Status of the Claims

Upon entry of this Amendment, claims 1, 4-7, 21, 23-29 and 31-40 are pending. Claims 1, 4-7, 21, 23-25, 28, 29 and 38 have been examined. Claims 2, 3, 8-20, 22 and 30 have been cancelled without prejudice or disclaimer. Claims 26, 27 and 31-37 have been withdrawn from examination by the Examiner as being directed to non-elected subject matter. Claims 1, 24, 25, 28, 29 and 38 have been amended without prejudice or disclaimer. Claims 39 and 40 have been added.

Claims 1, 24 and 25 have been amended to delete the phrases "or being susceptible to" (cancer) and "and prodrug" and to recite that X^1 and X^2 are independently selected from hydroxyl (-OH) and acetoxy (-OAc). Support for the amendments is found throughout the specification, e.g., at page 14, lines 13-15; page 18, lines 7-9; the compounds set out on pages 23-28; and original claim 8.

Claims 24 and 25 have been amended to include the proviso that R^1, R^2 and R^3 are not all hydrogen. Support for the proviso is found in the specification at, for example, page 15, line 28. (N.B.: The respective positions in Formula IIa and IIb set out in claims 24 and 25 that correspond to "R^4" are hydrogen. Accordingly, the recitation in claims 24 and 25 that "R^1, R^2 and R^3 are not all hydrogen" is equivalent to the recitation in the specification that "R^1, R^2, R^3 and R^4 are not all hydrogen.")

Claim 28 has been amended to comport with the amendment to claim 1 and to cancel non-elected subject matter.

Claims 29 and 38 has been amended for clarity.

Support for new claims 39 and 40 is found in original claims 12 and 13.

By this Amendment, no new matter has been added the application.

II. Response to Rejections

The rejections set out in the Office Action are summarized and addressed as follows.

(i) Rejection Under 35 U.S.C. §112, second paragraph

Claim 29 was rejected as indefinite for recitation of the phrase "the medicament." In response, claim 29 has been amended. The basis for the rejection is believed to have been addressed and overcome. Reconsideration of claim 29 and withdrawal of the rejection under 35 U.S.C. §112, second paragraph is requested.

(ii) Rejections Under 35 U.S.C. §112, first paragraph

Claims 1, 4-8, 21, 23-25, 28, 29 and 38 were rejected both for alleged lack of written description and for alleged lack of enablement. The basis of the rejections was the inclusion of "prodrugs" within the scope of the claims. The Examiner's position that the specification does not describe or enable "prodrugs" of the compounds recited in the claims is not well taken. The specification discloses compounds of formula I wherein X^1 and/or X^2 are acetoxy (-OAc). One of ordinary skill in the art would recognize that an acetoxy group may be a prodrug for a hydroxyl group (a recited alternative for X^1 and/or X^2). Based on this disclosure and other disclosure set out in the specification, one of ordinary skill in the art would understand the inventors had possession of "prodrugs" when the application was filed and, additionally, that "prodrugs" are fully enabled by the specification.

Notwithstanding Applicants' assertion that the specification enables and provides written description for "prodrugs" and without conceding the validity of the rejections, solely to advance prosecution of the application, claims 1, 24 and 25 have been amended. The term "prodrugs" has been deleted from the claims. Claims 1, 24 and 25 have further been amended to recite "X^1 and X^2 are independently selected from hydroxy (-OH) and acetoxy (-OAc)."

The basis for the enablement and written description rejections has been addressed and overcome. The specification enables and provides written description for the full scope of the claims. Reconsideration of the claims and withdrawal of all rejections under 35 U.S.C. §112, first paragraph is requested.

(iii) Rejection Under 35 U.S.C. §103

Claims 1, 4-8, 21, 23-25, 28 and 38 were rejected as being allegedly obvious over Halperin et al., US 2007/0099976 A1 ("Halperin"). In response, without conceding the validity of

the rejection, the claims have been amended to be directed to compounds of formulas I, IIa and IIb wherein X^1 and X^2 are independently selected from hydroxy (-OH) and acetoxy (-OAc) and the proviso that R^1, R^2 and R^3 and (in the case of formula I) R^4 are not all hydrogen. *See* claims 1, 24 and 25. For at least the reasons set out below, the amended claims are not obvious over Halperin.

With regard to compounds wherein X^1 and X^2 are hydroxyl, the Examiner asserts that the elected species (Compound 41) is obvious over Halperin's Compound 1259 in Table 6 and the disclosure of compounds substituted at the 4, 5, 6 or 7 position of the phenyl ring with halogens, including fluorine (*citing* Halperin, Table 1) and the Halperin's disclosure of a generic formula wherein R^1 and R^2 can both be halogen (among dozens of other possibilities). The Examiner identifies Halperin's Compounds 1350 (Table 1) and 1259 (Table 6) as representing the compounds closest in structure to Applicants' elected compound.

The amended claims are not obvious over Halperin. In chemical cases, a finding of obviousness requires identification of a lead compound that one of ordinary skill in the art would choose as a starting point to arrived at the claimed invention. *Eisai Co. Ltd. v. Dr. Reddy's Laboratory,* 533 F.3d 1353, 1357 (Fed. Cir. 2008); *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.,* 492 F.3d 1350, 1356 (Fed. Cir. 2007). A finding of obviousness further requires a rationale to modify the prior art to arrive to arrive at the claimed invention and a reasonable expectation of success for making the modification. *See KSR Int'l. Co. v. Teleflex Inc.,* 550 U.S. 398, 418 (2007), *quoting In re Kahn,* 441 F.3d 977, 988 (Fed. Cir. 2006); *Pfizer v. Apotex,* 480 F.3d 1348, 1364 (Fed. Cir. 2007), *citing Merck & Co. v. Biocraft Labs., Inc.,* 874 F.2d 804, 809 (Fed. Cir. 1989), *cert. denied,* 493 U.S. 975 (1989); *In re O'Farrell,* 853 F.2d 894, 903 (Fed. Cir. 1988). Here, one of ordinary skill in the art would find no rationale to choose a compound in Halperin that should or could be modified to a compound wherein X^1 and X^2 are independently selected from hydroxy (-OH) and acetoxy (-OAc) and the proviso that R^1, R^2 and R^3 and (in the case of formula I) R^4 are not all hydrogen. Halperin thus does not suggest the compounds called for in the subsisting claims and the claims are therefore not obvious over Halperin.

First, there would be no reason to choose Halperin's compound 1259 as a starting point to arrive at the compounds called for in the instant claims because Halperin teaches that compound 1259 has poor activity in assays used to predict inhibition of translation and/or treating,

e.g., proliferative disorders. As noted by the Examiner, compound 1259 comprises 3, 3-bis-(4-hydroxy-phenyl) substituents. This substitution pattern corresponds to X^1 and X^2 of the compounds specified in claims 1, 24 and 25. Halperin discloses that, when tested, compound 1259 caused no depletion of intracellular calcium stores (*see* "-" result reported in "Ca^{2+}" column in Table 6) and that compound 1259 further did not exhibit any relevant ability to reduce cell growth of A549 lung cancer cells (*see* value of ">20" in column "SRB" in Table 6). Other compounds set out in Table 6 exhibited activity in the calcium-depletion assay and the ability to reduce cell growth of the A549 lung cancer cells. No other compound set out in Table 6 had both a negative result in the calcium depletion assay and failed to reduce cell growth of A549 lung cancer cells at the test concentrations. (Halperin failed to even test the ability of compound 1259 to phosphorylate eIF2α.)

Upon considering the results set out in Table 6, one of ordinary skill in the art would thus conclude that compound 1259 was one of the least promising compounds within the series (and quite possibly the absolute least promising compound within the series). One of ordinary skill in the art would thus not choose compound 1259 as starting point to obtain additional compounds with activity for, e.g., inhibiting proliferative growth. To the contrary, upon considering the results set out in Table 6, one of ordinary skill in the art would view Halperin as teaching away from the compounds wherein the substituents in the 4-positions of the phenyl rings are hydroxyl (corresponding to X^1 and X^2 of the present claims).

Nor, in view of the results reported for compound 1259, would one ordinary skill in the art start find any motivation to modify Halperin's compound 1350 to arrive at the instant claims. Modification of compound 1350 to arrive at the compounds called for in the instant claims would require addition of hydroxyl groups to form the 3,3-bis-(4-hydroxy-phenyl) derivative that is found in compound 1259. As discussed above, such a 3,3-bis-(4-hydroxy-phenyl) derivative was the least promising of any compound listed in Table 6. All of the other compounds in Table 6 had performed better in one or more activity assay, compared to compound 1259. There would thus be no motivation modify compound 1350 to arrive at the compounds of the instant claims by examining all of the possible substituents for R_1 and R_2 in Halperin and choosing hydroxy groups for both R_1 and R_2.

For the reasons set out above, it would not have been obvious to modify Halperin's compounds that the Examiner has identified as the closet prior art to arrive at the compounds called for in the instant claims. The claims are thus not obvious over Halperin. Reconsideration and withdrawal of the rejection of the claims as obvious over Halperin is requested.

Claim 29 has been rejected as allegedly obvious over Halperin in view of Brugnara, et al., WO 99/26611 ("Brugnara"). The Examiner applics Halperin as set forth above and cites Brugnara solely for the proposition that it would allegedly be obvious to administer Halperin's compounds with other chemotherapeutic agents. Brugnara thus has no direct relevance to the compounds recited in the instant claims. Accordingly, Brugnara cures none of the Halperin's deficiencies in suggesting the compounds recited in the subsisting claims. The claims are therefore not obvious over Halperin in view of Brugnara. Reconsideration of claim 29 and withdrawal of the rejection over Halperin in view of Brugnara is requested.

For all of the reasons set forth above, the claims are not obvious over the prior art of record. Reconsideration of the claims and withdrawal of all rejections under 35 U.S.C.§103 is requested.

III. New Claims

It is axiomatic that if an independent claim is patentable over the prior art, all claims that depend directly or indirectly from the independent claim are also patentable over the prior art. New claims 39 and 40 are dependent claims that rely on claim 1 as their base claim. Claims 39 and 40 are thus patentable over the prior art for at least the same reasons that claim 1 is patentable over the prior art. Furthermore, claims 39 and 40 are believed to comply with all requirements for patentability set out in 35 U.S.C. §§101 and 112. Allowance of claims 39 and 40 is requested.

IV. Conclusion

All rejections have been addressed and overcome. The application is believed to be in condition for allowance, which is earnestly solicited.

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